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Novel antimicrobial drugs based on complex chitosan salts with chiral organic ligands

© **Anna B. Shipovskaya**,[1,2]*+ **Irina V. Zudina**,[2] **Valentina I. Fomina**,[2] and **Olga N. Malinkina**[1,2]
[1] *Basic Chair of Polymers. Institute of Chemistry. Saratov State University. Astrakhanskaya St., 83. Saratov, 410012. Russia. Phone: +7 (8452) 51-69-57. E-mail: ShipovskayaAB@rambler.ru*
[2] *Department of Macromolecular Compounds. Education and Research Institute of Nanostructures and Biosystems. Saratov State University. Astrakhanskaya St., 83. Saratov, 410012. Russia. Phone: +7 (8452) 21-07-59. E-mail: Olga-Malinkina@yandex.ru*

*Supervising author; +Corresponding author
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Abstract

The processes of salt formation and gelation in the system of hydrochloride chitosan + ascorbic acid + water were investigated by elemental analysis, potentiometric titration, spectropolarimetry, IR and NMR spectroscopy. It has been established that the interaction of these components in an aqueous medium followed by formation the hydrogel of complex chitosan salt with an inorganic (chloride) and a chiral organic ligand (ascorbate). The viscometric and rheological properties of hydrochloride-ascorbate chitosan aqueous solutions were studied. There were shown a polyelectrolyte effect of polysalt macromolecules in dilute solutions and a typical non-Newtonian fluid flow pattern in concentrated solutions. A substantial effect on these properties by the isomeric form of the chiral organic anion (*L*- or *D*-), the temperature and storage time of the hydrogel composition was noted. Our studies suggest that the junctions in the hydrogel grid of chitosan binary salt are formed by a system of complex ion-ion and hydrogen contacts between the macromolecules and the organic acid molecules. The antibacterial action against opportunistic pathogens of these hydrogels based on hydrochloride-ascorbate salts of chitosan was established by *in vitro* and *in vivo* methods. The dynamics of changes in the content of cytokines (TNF-α, IL-1β) in the periodontal pocket fluid in patients with inflammatory diseases of their periodontal tissues was studied when the gingiva treated by our chitosan polysalt hydrogel. It was found that the drug exhibited a pronounced anti-inflammatory activity, apparently due to the regulation of cytokines IL-1β and TNF-α in inflammation. The revealed patterns show that the therapeutic effect of our hydrogels is caused not only by the prolonged readjustment of the periodontal pockets but also by the immunotropic action upon the effectors of innate immunity. The mechanism of action of complex chitosan salts with a chiral organic ligand on live cells is apparently the same as that of polycationic antimicrobial proteins, primarily β defensins.